

ART. XVI.—*On the Synthesis of Sugars from Formaldehyde,
Carbon Dioxide and Water.*

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[Read 7th November, 1918].

In the Proceedings of the Royal Society of Victoria, Vol. 30, 1918, p. 200, a method was described of producing sugar from formaldehyde by the joint action of boiling lime water and sodium hydrate on formaldehyde. In the earlier experiments the by-products were mainly calcium tartrate and sodium formate. In later experiments the by-products were calcium carbonate and calcium and sodium formates. The formaldehyde first used was a sample of Merck's, purchased before the outbreak of war, and used in preference because of its supposed greater purity. It seems probable, however, that the appearance of tartaric acid was due to the formaldehyde having undergone slow oxidation prior to use, possibly in the presence of a trace of some metallic or other oxidase, or of some accidental contamination. It is well known that nitric acid, for instance, will slowly oxidize ordinary aldehyde (acetaldehyde) to glyoxal, from which tartaric acid is readily synthesized, as for instance by the addition of hydrocyanic acid, and subsequent treatment with dilute mineral acid. Tartaric acid is also readily oxidized to formic acid, and hence the reaction might be reversible. Attempts to synthesize tartaric acid from formic acid by passing CO_2 into a boiling solution of a formate containing reducing agents (powdered Mg.) and oxidizing agents (H_2O_2 , HNO_3), failed, as was also the case when formates, Mg, CO_2 and water were kept under pressure for long periods of time.

Similarly formaldehyde subjected to the slow and rapid action of a variety of oxidizing agents at varying temperatures (HNO_3 , H_2O_2 , $\text{K}_2\text{Cr}_2\text{O}_7$, K_4Cfy , K_3Cfy , etc.), failed to yield any tartaric acid when used for sugar synthesis. The statements made in the note first published must therefore be modified in two respects, namely: no tartrates are produced, and the resultant liquid is optically inactive instead of showing a slight optical activity.

The purpose of the present work was to determine the best condition for the synthesis of sugars from formaldehyde and to obtain

a comprehensive view of the different agencies by which such synthesis could be brought about, and the relationship between them. In the first instance the action was tested of alkaline metallic hydroxides and carbonates, and then of non-metallic alkalis.

Alkaline metallic hydroxides.

Caustic Soda. If strong caustic soda is run into boiling 40 % formaldehyde until the liquid ceases to smell of the latter, sodium formate is produced, but no reducing sugar. If 30 c.c. of 40 % CH_2O and 14 c.c. of 33 % NaHO are boiled to dryness in a flask with a narrow outlet, the residue consists of nearly pure sodium formate, only a trace of matter is removed by alcohol, and this contains no reducing sugar.

If, however, while the evaporation is going on, hot water is added several times, the residue contains a small trace of reducing sugar removed by washing with 96 to 98 % alcohol.

If 30 c.c. of 40 % CH_2O are added to 500 c.c. of water and 40 c.c. of 10 % NaHO , and the bulk of the liquid dripped slowly into a boiling portion, the liquid continues to smell of CH_2O until nearly dry, and the pale yellow residue contains an appreciable amount of reducing sugar but consists mainly of sodium formate.

If more soda is added during boiling all the CH_2O disappears, and the amount of reducing sugar is increased, but any excess of soda turns the liquid dark brown.

Further experiments showed that with increasing dilution the proportion of sugar to sodium formate increased, but that the latter was always formed in excess.

Lime-water.—100 c.c. of Lime-water were added to 25 c.c. of 40 % formaldehyde, and while boiling in a flask fitted with a condensing arrangement, lime-water was run in slowly until all the CH_2O was used up. Approximately, 1 litre of lime-water was required. The pale yellow syrup yielded calcium formate when evaporated, methyl alcohol escaped, and the gummy residue contained a high proportion of reducing sugar, largely pentose and giving the phloroglucin reaction readily. The amount of sugar was considerably less than with the joint action of sodium hydrate and calcium hydrate as previously described.

Barium and Strontium hydrates.—With Barium hydrate, to complete the reaction an excess of the alkali is required and prolonged boiling. Strontium hydrate is more active, only a slight excess is necessary, and moderately prolonged boiling (2-4 hours

with 5 grains of $\text{Sr H}_2\text{O}_2$, 25 c.c., 40 % CH_2O and 500 c.c. water). Soluble Barium and Strontium formates are produced, and the reducing sugars contain a high proportion of a pentose sugar resembling arabinoketose, and less soluble in 95 % alcohol than the hexoses.

Magnesium hydrate.—To complete the reaction an excess is required, and either 2 days' heating on a water bath, or 4 to 6 hours' boiling. Magnesium formate is produced, and the reducing sugars give an abundant precipitate of golden yellow needles with phenylhydrazin. Most of these resembled the bundles produced with arabinoketose, but a smaller proportion appeared to correspond to a glucosazone.

Ammonium hydrate.—Ammonia directly combines with formaldehyde to form urotropin. If magnesium powder is added, ammonia slowly escapes, formaldehyde reappears, and magnesium formate is slowly formed, and the residue is black instead of white. After 3 months at 12°C ., the filtered liquid blackens with sulphuric acid, but contains no reducing sugar. The formaldehyde present is, however, partly converted into reducing sugar by prolonged boiling with Magnesium hydrate.

This observation shows that the Magnesium of chlorophyll might be able to liberate formaldehyde from a non-volatile temporary storage combination for subsequent polymerization to sugar.

Alkaline carbonates.—If 10 % Na_2CO_3 is dripped slowly into boiling 5 % CH_2O , the reaction lags considerably, and an excess of Na_2CO_3 is always present by the time all the CH_2O has disappeared. This causes the syrup to turn brown. Using 2 grams of Na_2CO_3 to 20 c.c. of 40 % CH_2O and 200 c.c. of water, the reaction was completed after 2 hours' boiling. Using 0.5 grams of Na_2CO_3 , prolonged boiling was needed to complete the reaction, and a small trace of Na_2CO_3 still remained; less sugar was formed.

The addition of absolute alcohol to the syrup precipitates the sodium carbonate remaining, and a second addition of alcohol after concentrating to a small bulk precipitates nearly all the sodium formate. A second repetition leaves a solution of a nearly pure mixture of reducing sugars, containing both pentoses and hexoses.

Potassium carbonate acts similarly to sodium carbonate, but is much less active, prolonged boiling being necessary, with an excess of the carbonate. The bi-carbonate is still less active, but the products are the same, namely, sodium formate, methyl alcohol, and reducing sugars.

Calcium carbonate.—H. and A. Euler (Ber. d. D. Bot. Ges., 1906, 39, pp. 36 and 39), have shown that when 2 % formaldehyde is heated with calcium carbonate, a pentose sugar, arabinoketose is formed, together with small amounts of glycollic aldehyde and dihydroxyacetone.

The calcium carbonate is converted into calcium formate, and the reaction is possible because a portion of the former exists in solution as calcium hydrate. As this is converted into formate CO_2 escapes and more chalk dissociates. Hence the rapidity of the action depends upon the fineness of division of the chalk. Thus using 5 c.c. of 40 % CH_2O to 250 c.c. water, and a slight excess of chalk, the following were the times taken for the removal of all the formaldehyde:—

Finely divided, freshly pptd. chalk, 70 hours' boiling.

Coarser portion of precipitate, 82 hours' boiling.

Dried precipitated chalk, 96 hours' boiling.

In all cases the liquid is pale yellow by the second day, and is distinctly browned by the time the reaction is completed. Presumably this is due to the presence of traces of dissociated lime-caramelizing the sugar produced.

The syrup was evaporated to a small bulk, filtered, diluted and kept for 3 days at 30°C . (a) with dry yeast, (b) with fresh yeast and Pasteur's ash. Bacteria became abundant in (b). Both liquids yielded a distillate which gave the iodoform test for alcohol faintly but distinctly, but which did not contain sufficient alcohol to affect the boiling point appreciably. Evidently, however, traces of hexose sugars, fermentable by yeast, are formed in addition to arabinoketose.

Magnesium carbonate is feebly alkaline, more soluble, and dissociates more readily than calcium carbonate in solution. Hence it reacts more rapidly. Using half a gram to 5 c.c. of 40 % CH_2O and 250 c.c. of water, the reaction was completed in 4 hours boiling with magnesia alba levis, and in 12 hours with magnesia alba ponderosa.

Barium carbonate.—Using a slight excess of the solid and 5 c.c. of 40 % formadehyde the reaction was completed—

With 400 c.c. of water in 16 hours' boiling.

With 250 c.c. of water in 36 hours' boiling.

The sugars appeared to be the same as with calcium carbonate, but possibly owing to the difficulty of separating all traces of the poisonous barium formate even by the use of sulphuric acid, the tests with yeast were inconclusive.

Strontium carbonate.—Using 5 c.c. of 40 % CH_2O to 250 c.c. of water the reaction was completed with—

Freshly precipitated carbonate in 52 hours' boiling.

Ppt. dried, and then powdered, in 130 hours' boiling.

Large excess of fresh precipitate, in 30 hours' boiling.

The explanation is that the large excess contains more finely divided particles, which dissolve and dissociate more rapidly, and hence the rapidity of the reaction is greater. With similar materials there is, in fact, a relation between the solubility and the rates of reaction of calcium, barium and strontium carbonates with formaldehyde.

	CaCO_3 .	SrCO_3 .	BaCO_3 .
Solubility in boiling water	18	53	66
Hours boiling required to complete reaction	70	52	36
Ratio of products	12	27	23

The barium and strontium carbonates are, however, not only more soluble, but about twice as chemically active as calcium carbonate.

Sodium formate is itself feebly alkaline. Hence the effect of boiling it with formaldehyde solutions of varying strengths was tried. The sodium formate was added directly, or a small amount at a time, and at atmospheric pressure and under pressures up to 15 atmospheres. In no case was any sugar produced. Potassium formate also gave negative results. Apparently the polymerization of sugar from formaldehyde is not induced merely by boiling in an alkaline solution, but requires also the presence of an alkaline base capable of combining with formic acid as fast as it is formed.

Sodium phosphate.— Na_3PO_4 . After boiling 1 % formaldehyde with strongly alkaline 5 % sodium phosphate for 3 days, the liquid became almost neutral, was pale brown in colour, and contained a small quantity of reducing sugar. Apparently the alkaline sodium phosphate forms Na_2HPO_4 , and the free soda produces sodium formate and polymerizes a little of the formaldehyde.

Non-metallic alkalis.—These are also capable of inducing the polymerization of formaldehyde to sugar.

Trimethylamine is strongly alkaline. 5 c.c. of 40 % CH_2O were boiled with 8 c.c. of Trimethylamine and 400 c.c. of water for 50 hours in a condensing flask, and the pale brown liquid evaporated to dryness. The residue was extracted with water, again boiled to dryness, and extracted with absolute alcohol. The latter left a

gummy residue of reducing sugar, apparently mainly or wholly pentose.

Aniline water is feebly alkaline. It gives a dense white precipitate with formaldehyde in concentrations down to 0.05 %. The white ppt. formed by adding 500 c.c. of saturated aniline water to 50 c.c. of 1 % formaldehyde smells of the latter even after 3 days' boiling. On evaporating to dryness and extracting the resinous residue (which is probably an analogous compound to Bakelite) with water, a trace of reducing pentose sugar was obtained.

The joint action of alkalis.

Since a mixture of caustic soda and lime appears to be more effective in polymerizing formaldehyde to sugar than either singly, it seemed worth while to try the effect of lime produced directly in the boiling formaldehyde. A preliminary experiment performed by added 5 % caustic soda to 250 c.c. of boiling 1.6 % formaldehyde containing in one case 0.8 % calcium chloride, and in the other no calcium chloride showed that all the formaldehyde was converted into formates and sugar in the first case with an addition of 13 c.c. of sodium hydrate, and in the other of 24.5 c.c., while the amount of sugar formed was approximately three times greater in the former case. The other products were calcium formate and sodium chloride.

To determine the best concentration for the reaction, 5 c.c. of 40 % formaldehyde and 5 c.c. of 17 % calcium chloride (anhydrous) were added to varying amounts of water, and 3.5 % sodium hydrate run into the boiling mixture until the reaction was completed.

Amount of Water present.	-	Amount of 3.5% NaHO required.
35 c.c.	-	11.8 c.c.
60 c.c.	-	9.9 c.c.
110 c.c.	-	8.7 c.c.
260 c.c.	-	8.0 c.c.
510 c.c.	-	9.8 c.c.
760 c.c.	-	10.2 c.c.
1010 c.c.	-	11.4 c.c.

The concentration represented by the addition of 250 c.c. appears to be the best.

Hence using 5 c.c. of 40 % formaldehyde in 250 c.c., and adding varying amounts of Calcium chloride, the amounts of caustic soda required to complete the reaction were:—

	Amount of 3.5% Caustic Soda required.
With 17% calcium chloride—	
0.0 c.c. - - - -	21.2 c.c.
2.0 c.c. - - - -	11.3 c.c.
3.0 c.c. - - - -	10.8 c.c.
4.0 c.c. - - - -	8.9 c.c.
5.0 c.c. - - - -	8.0 c.c.
8.0 c.c. - - - -	9.0 c.c.
10.0 c.c. - - - -	9.5 c.c.
With 15% NaCl—	
5.0 c.c. - - - -	20.8 c.c.
Solution saturated with NaCl. -	18.3 c.c.
0.8% calcium formate - - -	7.8 c.c.

Even using a condensing flask in which to carry the reaction, the amount of soda required varies by a fraction of a cubic centimeter when the tests are done in duplicate. The presence of calcium chloride lessens the amount of soda required up to a concentration of 0.34 %. Salt has no effect except when present in sufficient amount to raise the boiling point of the liquid. Calcium formate is as effective as calcium chloride, and its use has the advantage that both the salts produced are formates (calcium and sodium).

The following experiments indicate the effect of the presence of Magnesium, Barium and Strontium salts. In each case 5 c.c. of 40 % formaldehyde was used in 250 c.c. of water, and the sodium hydrate dripped slowly into the liquid boiling in a condensing flask.

25 c.c. of 2% Solution.	Amount of 3.5% NaHO to complete reaction.
Magnesium sulphate - - -	20.5 c.c.
Barium chloride - - -	14.1 c.c.
Water only - - -	22.0 c.c.
Strontium chloride - - -	15.7 c.c.
Water only - - -	21.9 c.c.

The reaction lags considerably, and if the addition of sodium hydrate is made rapidly, a white precipitate is apt to form, particularly in the case of the magnesium, which only redissolves slowly, in the form of a soluble formate.

Hence the presence of a magnesium salt exercises little or no catalytic action on the polymerization of formaldehyde to sugar by caustic soda, and Barium and Strontium salts are less effective than calcium salts.

The influence of temperature.

Not only is dilution a condition for the abundant polymerization of formaldehyde to sugar by alkalies, but also a high temperature. Thus using Barium hydrate and 1 % per cent. formaldehyde the times required to complete the reaction on a water bath at 80° C., boiling at 100° C., and in an autoclave at 110° C., were respectively 5, 3 and 1.

In addition, however, at low temperatures less and less sugar is produced, and finally only formates. Thus Barium hydrate kept in contact with 10 %, 4 % and 2 % formaldehyde for 3 months at 10-12° C., in sealed receptacles, was partly converted into Barium formate and some methyl alcohol and barium carbonate appeared, but no reducing sugar.

Similarly 250 c.c. water and 25 c.c. of 3.5 % NaHO and 5 c.c. of 40 % CH₂O after 3 months at 10° C. to 12° C., yielded sodium formate, but no reducing sugar, and a trace of CH₂O remained unaltered.

The same applies when sodium hydrate is used in conjunction with calcium chloride. Thus 500 c.c. of water, 10 c.c. of 40 % CH₂O, 10 c.c. of 17 % CaCl₂, and 15.5 c.c. of 3.5 % sodium hydrate after 3 months at 12° C., the liquid still contained CH₂O, but was practically neutral to litmus and feebly alkaline to phenolphthalein (as in the case of dilute sodium formate), is contained no reducing sugar and calcium and sodium chlorides and formates, mainly as calcium chloride and sodium formate. In some similar tests, using double the quantity of formaldehyde, a trace of reducing sugar appeared, but only a mere trace, and the products otherwise were the same.

Tests for fermentable synthesized sugars.—Large samples of crude sugar were obtained from formaldehyde by the use of calcium formate and caustic soda. The concentrated and filtered syrup was diluted and fermented for three days at 30° C. with dry yeast and with fresh yeast after the addition of Pasteur's ash. The fresh yeast showed signs of budding and increased in amount. A fair quantity of carbon dioxide was formed. The distillate gave the iodoform test for alcohol readily and contained between 3 and 4 % of alcohol. The residual liquid after distillation contained a large amount of reducing sugar. It was optically inactive, and formed a good culture medium for various Bacilli and for *Penicillium* and *Eurotium*, particularly with the addition of Pasteur's ash.

Cultures supported fresh crops of fungi for weeks, but remained optically inactive throughout.

Chemosynthesis of sugar from CO_2 and water.—It is well known that powdered magnesium will cause traces of formaldehyde to appear slowly in a solution of carbon dioxide in water. 250 c.c. of water with 2 grains of Magnesium were charged with carbon dioxide under pressure for 3 weeks at 12 to 15° C., and then boiled in a condensing flask for 2 days. After then boiling to a small bulk and filtering, the filtrate was evaporated nearly to dryness and excess of hot absolute alcohol added. The filtrate on evaporating to dryness left a gummy residue readily soluble in water, optically inactive and containing reducing hexose and pentose sugar, one of the former being apparently a levulose and giving the ketohexose test with resorcin, while the pentose gives the usual precipitate with phloroglucin and HCl soluble in amyl alcohol.

Summary.

The polymerization of formaldehyde to sugar by alkalies and alkaline carbonates has been investigated.

The main conditions for a high proportion of sugar are appropriate dilution and a temperature of 100° C. to 110° C. The by-products are formates and methyl alcohol mainly. At low temperatures little or no sugar is produced.

The most rapid reaction is produced by sodium hydrate. In the presence of a neutral calcium salt, the amount of sugar condensation is greatly increased, less alkali is required and less formate produced. Neutral Barium and Strontium salts are less effective as condensing catalytic agents.

The best method is by running 7 to 8 c.c. of 3.5 % sodium hydrate into 250 c.c. of 0.8 % calcium formate containing 5 c.c. of 40 % formaldehyde while boiling in a condensing flask. The reaction is completed in a few minutes, and as soon as a pale yellowish tinge appears, all the formaldehyde has disappeared.

The sugar mixture is optically inactive, and contains reducing pentoses and reducing fermentable hexoses. Carbon dioxide and water are readily polymerized to sugar by the aid of magnesium. The production of calcium tartrate during sugar synthesis has not been confirmed, and was possibly due to the use of an oxidized sample of formaldehyde.